

WHAT IS CLAIMED IS:

- 1 1. An isolated nucleic acid encoding a polypeptide comprising an
2 alpha subunit of a KCNQ potassium channel, the polypeptide:
3 (i) forming, with at least one additional KCNQ alpha subunit, a
4 KCNQ potassium channel having the characteristic of voltage-gating; and
5 (ii) comprising a subsequence having at least 65% amino acid
6 sequence identity to amino acids 343 to 640 of SEQ ID NO:4.
- 1 2. The nucleic acid of claim 1, wherein the polypeptide specifically
2 binds to antibodies generated against SEQ ID NO:4 or SEQ ID NO:5.
- 1 3. The nucleic acid of claim 1, wherein the polypeptide encodes
2 human KCNQ5.
- 1 4. The nucleic acid of claim 1, wherein the nucleic acid encodes an
2 amino acid sequence of SEQ ID NO:4 or SEQ ID NO:5.
- 1 5. The nucleic acid of claim 1, wherein the nucleic acid comprises a
2 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.
- 1 6. The nucleic acid of claim 1, wherein the nucleic acid is amplified
2 by primers that selectively hybridize under stringent hybridization conditions to the same
3 sequence as the primers selected from the group consisting of:
4 CCACGTCTGCACTCAGGAAGTCTCCG (SEQ ID NO:6)
5 CCAGCTTGGATTCTATGGACTGTACC (SEQ ID NO:7)
6 GAAGAGCCGAGAGAAAATAACAGCAG (SEQ ID NO:8)
7 GCCCTGTGGATAGCAAGATCTTTCG (SEQ ID NO:9)
8 GCTGTGAGCATAAACC ACTGAACCC (SEQ ID NO:10)
9 CCATGCGCACCATGCGGAGGATCTG (SEQ ID NO:11)
10 CATGAAGGATGTGGAGTCGGG (SEQ ID NO:12) and
11 TGGCTAAAGAACTGCTATGCCTGG (SEQ ID NO:13).
- 1 7. The nucleic acid of claim 1, wherein the polypeptide encoded by
2 the nucleic acid comprises an alpha subunit of a homomeric potassium channel.

1 8. The nucleic acid of claim 1, wherein the polypeptide encoded by
2 the nucleic acid comprises an alpha subunit of a heteromeric potassium channel.

1 9. The nucleic acid of claim 1, wherein the nucleic acid selectively
2 hybridizes under moderately stringent hybridization conditions to a nucleotide sequence
3 of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

1 10. An isolated nucleic acid encoding a KCNQ polypeptide, the
2 nucleic acid specifically hybridizing under stringent conditions to a nucleotide sequence
3 of SEQ ID NO:1, SEQ ID NO:2, or SEQ ID NO:3.

1 11. An isolated nucleic acid that specifically hybridizes under stringent
2 conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO:4 or SEQ
3 ID NO:5.

1 12. A method of detecting a nucleic acid, the method comprising
2 contacting the nucleic acid with an isolated nucleic acid of claim 1.

1 13. An isolated polypeptide comprising an alpha subunit of a KCNQ
2 potassium channel, the polypeptide:

3 (i) forming, with at least one additional KCNQ alpha subunit, a
4 KCNQ potassium channel having the characteristic of voltage-gating; and

5 (ii) comprising a subsequence having at least 65% amino acid
6 sequence identity to amino acids 343 to 640 of SEQ ID NO:4.

1 14. The polypeptide of claim 13, wherein the polypeptide specifically
2 binds to antibodies generated against SEQ ID NO:4 or SEQ ID NO:5.

1 15. The polypeptide of claim 13, wherein the polypeptide has a
2 molecular weight of between about 95 kD to about 104 kD.

1 16. The polypeptide of claim 13, wherein the polypeptide has an amino
2 acid sequence of human KCNQ5.

1 17. The polypeptide of claim 13, wherein the polypeptide has an amino
2 acid sequence of SEQ ID NO:4 or SEQ ID NO:5.

1 18. The polypeptide of claim 13, wherein the polypeptide comprises an
2 alpha subunit of a homomeric potassium channel.

1 19. The polypeptide of claim 13, wherein the polypeptide encoded by
2 the nucleic acid comprises an alpha subunit of a heteromeric potassium channel.

1 20. An antibody that specifically binds to the KCNQ polypeptide of
2 claim 13.

1 21. The antibody of claim 20, wherein the polypeptide to which the
2 antibody binds has an amino acid sequence of SEQ ID NO:4 or SEQ ID NO:5.

1 22. An expression vector comprising the nucleic acid of claim 1.

1 23. A host cell transfected with the vector of claim 22.

1 24. A method for identifying a compound that increases or decreases
2 ion flux through a potassium channel, the method comprising the steps of:

3 (i) contacting the compound with a KCNQ polypeptide, the polypeptide

4 (a) forming, with at least one additional KCNQ alpha subunit, a
5 KCNQ potassium channel having the characteristic of voltage-gating; and

6 (b) comprising a subsequence having at least 65% amino acid
7 sequence identity to amino acids 343 to 640 of SEQ ID NO:4; and

8 (ii) determining the functional effect of the compound upon the potassium
9 channel.

1 25. The method of claim 24, wherein the functional effect is a physical
2 effect.

1 26. The method of claim 24, wherein the functional effect is a chemical
2 effect.

1 27. The method of claim 24, wherein the polypeptide is expressed in a
2 eukaryotic host cell or cell membrane.

1 28. The method of claim 27, wherein the functional effect is
2 determined by measuring ion flux, changes in ion concentrations, changes in current or
3 changes in voltage.

1 29. The method of clam 24, wherein the functional effect is determined
2 by measuring ligand binding to the channel.

1 30. The method of claim 24, wherein the polypeptide is recombinant.

1 31. The method of claim 24, wherein the potassium channel is
2 homomeric.

1 32. The method of claim 24, wherein the potassium channel is
2 heteromeric.

1 33. The method of claim 24, wherein the polypeptide is human KCNQ5

1 34. The method of claim 24, wherein the polypeptide has an amino acid
2 sequence of SEQ ID NO:4 or SEQ ID NO:5.

1 35. A method of modulating ion flux through a KCNQ potassium
2 channel, the method comprising the step of contacting the KCNQ potassium channel,
3 wherein the channel comprises a KCNQ5 alpha subunit, with an therapeutically effective
4 amount of a compound identified using the method of clam 24.

36. A method for identifying a compound that increases or decreases ion flux through a potassium channel comprising a KCNQ5 polypeptide, the method comprising the steps of:

4 (i) entering into a computer system an amino acid sequence of at least 50
5 amino acids of a KCNQ5 polypeptide or at least 150 nucleotides of a nucleic acid
6 encoding the KCNQ5 polypeptide, the KCNQ5 polypeptide comprising a subsequence
7 having at least 65% amino acid sequence identity to amino acids 343 to 640 of SEQ ID
8 NO:4;

9 (ii) generating a three-dimensional structure of the polypeptide encoded by
10 the amino acid sequence;

11 (iii) generating a three-dimensional structure of the potassium channel
12 comprising the KCNQ5 polypeptide;
13 (iv) generating a three-dimensional structure of the compound; and
14 (v) comparing the three-dimensional structures of the polypeptide and the
15 compound to determine whether or not the compound binds to the polypeptide.

1 37. A method of detecting the presence of hKCNQ5 in human tissue,
2 the method comprising the steps of:

3 (i) isolating a biological sample;
4 (ii) contacting the biological sample with an hKCNQ5-specific
5 reagent that selectively associates with hKCNQ5; and,
6 (iii) detecting the level of hKCNQ5-specific reagent that
7 selectively associates with the sample.

1 38. The method of claim 37, wherein the hKCNQ5-specific reagent is
2 selected from the group consisting of: hKCNQ5-specific antibodies, hKCNQ5-specific
3 oligonucleotide primers, and hKCNQ5-nucleic acid probes.

1 39. In a computer system, a method of screening for mutations of a
2 human KCNQ5 gene, the method comprising the steps of:
3 (i) entering into the computer a first nucleic acid sequence
4 encoding a KCNQ5 polypeptide having a nucleotide sequence of SEQ ID NO:1, SEQ ID
5 NO:2, or SEQ ID NO:3, and conservatively modified versions thereof;
6 (ii) comparing the first nucleic acid sequence with a second nucleic
7 acid sequence having substantial identity to the first nucleic acid sequence; and
8 (iii) identifying nucleotide differences between the first and second
9 nucleic acid sequences.

1 40. The method of claim 39, wherein the second nucleic acid sequence
2 is associated with a disease state.

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